# Figuring Out Puzzling Animal Diseases

Animal disease research sometimes follows a predictable path of discovery, identification, test availability, and finally, prevention or cure. But other times, the path becomes a long and winding road. ARS scientists at the Animal Diseases Research Unit (ADRU) in Pullman, Washington, are working to put together the pieces of some tough-to-solve animal disease puzzles.

**Bison Viral Infection Tough To Control**

Malignant catarrhal fever (MCF)—a viral infection that is a leading cause of disease in American bison—is usually transmitted from sheep to bison and cattle. Vaccine development has been stymied because the virus will not grow in cell culture.

Microbiologist Hong Li, veterinary medical officer Naomi Taus, and others at ADRU, in collaboration with Lindsay Oaks at Washington State University and Donal O'Toole at the University of Wyoming, have discovered that the reason the virus won't grow in cell culture is that it undergoes several changes inside the animal's body. It targets specific cell types at different stages of its life cycle—a process called "cell tropism switching."

The viral replication cycle in sheep can be divided into three stages: entry, maintenance, and shedding. When entering sheep through the nasal route, the virus reaches the lung, where it replicates exclusively. Replication in sheep lung is required for the virus to change its cell tropism for the next stage—infecting lymphocytes, a type of immune cell. In this maintenance stage, the virus stays in the lymphocytes, circulating through the whole body with little replication. This type of infection is referred to as a "latent infection." During the shedding stage, the virus reactivates from the infected lymphocytes, targets specific cells in the nasal turbinates to complete its replication, and is then shed through sheep nasal secretions.

PEGGY GREB (D1730-1)


**Veterinary microbiologist Hong Li selects MCF virus-free sheep for a viral replication study.**

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**A sheep from a flock established and maintained to be free of MCF and OPP viruses.**

"Amazingly, the virus replicated in turbinate cells is not capable of reinfecting turbinate cells because it changes its cell tropism again," Li says.

This type of presto-chango trickery has been very effective at keeping the virus in circulation. "It also explains why it has been impossible to grow in cell culture—it's like trying to grow one organism in a cell culture designed for another organism," Li says. With the knowledge of how the virus replicates in sheep, scientists can now begin to find the right cell types to grow the virus in cell culture.

**Closer to a Vaccine**

Until such a culture becomes available, Li and his colleagues are exploring alternative avenues of developing a vaccine to protect bison and cattle from MCF. Working with colleagues from the USDA Animal and Plant Health Inspection Service's National Veterinary Services Laboratories, the group plans to use a particular MCF virus strain present in hartebeest and topi (African antelopes) that does grow in culture.

"The topi MCF virus does not cause disease in cattle (and hopefully not in bison). We are trying to insert genes from the sheep MCF virus into the topi virus in an effort to create a vaccine to protect bison and cattle from getting MCF," says Li. "Even though a vaccine isn't around the corner, we're much closer to

one than we were 5 years ago. Until a vaccine is developed, spatial separation is the only way to prevent infection in bison."

**Using Genetics To Diagnose and Predict Disease**

Another ruminant disease being investigated by scientists at ADRU is ovine progressive pneumonia virus (OPPV), which causes mastitis, respiratory distress, swelling of the knees (arthritis), and wasting in infected sheep. One in two U.S. sheep of open-range flocks are infected with OPPV, and it is believed to be mainly transmitted between adult sheep through respiratory secretions. OPPV slowly erodes producers' profits over the years by lowering average weaning weights of lambs and the average number of lambs produced.

The current method to control OPPV is to test sheep blood for either antibodies to the virus or OPPV concentration and then separate infected sheep from uninfected sheep. The problem is that many infected sheep never develop clinical disease symptoms. Says microbiologist Lynn Herrmann-Hoesing, "An OPPV test that predicts or determines which infected sheep will then go on to display clinical disease is highly sought."

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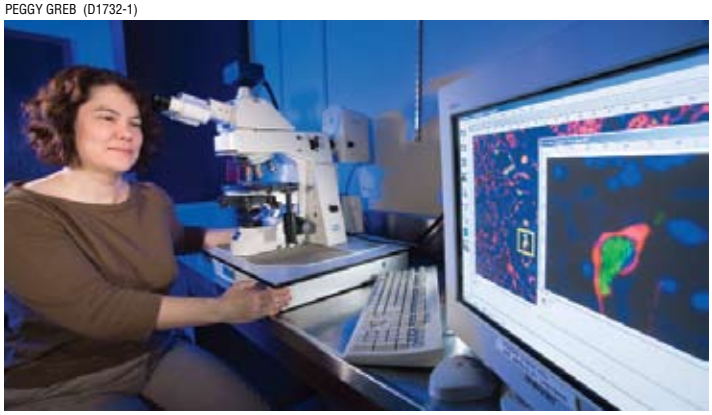

**Veterinary medical officer Naomi Taus examines an MCF virus-infected epithelial cell in a sheep lung. The red area is the virus, and the green area is the cell.**

Herrmann-Hoesing and geneticist Stephen White, in close collaboration with Michelle Mousel and Gregory Lewis of ARS's U.S. Sheep Experiment Station in Dubois, Idaho, are evaluating two different tests: One is a quantitative PCR test using real-time technology, and the second is an immunogenetics test.

"With one or both of these tests, we hope to provide a diagnostic method that determines or predicts whether the sheep will progress to OPPV clinical signs," says Herrmann-Hoesing. "In addition, these types of tests have the potential to significantly reduce the number of other tests necessary for determining infection and possibly lower the transmission potential in a flock. Therefore, these new tests offer significant long-term economic

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**Technician Shirley Elias (left) and veterinary medical officer Naomi Taus use a nebulizer to infect a sheep with MCF virus.**

advantages for the producer over conventional serological diagnostic tests."

Diagnostic testing of sheep can be expensive since current recommendations are to test annually or biannually for at least 5 years to ensure OPPV-negative flock status.

Animal diseases are a fact of life for livestock producers, but with improved diagnostic and therapeutic tools being investigated by ARS scientists, the well-being of food animals can be better managed and economic risks for the producers can be limited.—By **Sharon Durham,** ARS.

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PEGGY GREB (D1728-1)

**Animal care manager Emma Karel (left) and microbiologist Lynn Herrmann-Hoesing collect a blood sample from a sheep for an OPPV-related immunogenetic analysis.**